REMARKS

Applicants hereby submit that the enclosures fulfill the requirements under 37 C.F.R. §1.821-1.825. The amendments in the specification merely insert sequence identifiers in the specification and replace the original Sequence Listing with a substitute Sequence Listing. The substitute Sequence Listing contains the nucleic acid sequences depicted in Tables 1-8, and the amino acid sequences depicted in Table 9 and Figures 1-2. No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment.

Enclosed is a Petition for One-Month Extension of Time with a check in the amount of $110 for the petition fee.

Please apply any other charges or credits to Deposit Account No. 06-1050, referencing attorney docket number 12660-002001.

Respectfully submitted,

Date: September 23, 2002

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"Version With Markings to Show Changes Made"

In the specification:

Paragraph beginning at page 2, line 26, has been amended as follows:

Though the binding site on receptors associating with these cytoplasmic tyrosine kinases (JAK kinases) is conserved between family members, the homology is not very high (Murakami M. et al., Proc. Natl. Acad. Sci. USA, 1991, 88, 11349-11353). On one hand, the sequence that characterizes these hemopoietin receptors most well exists in the extracellular region, and especially the five amino acid Trp-Ser-Xaa-Trp-Ser (SEQ ID NO:32) (where Xaa is an arbitrary amino acid) motif is conserved in almost all of the hemopoietin receptors. Therefore, novel receptors are expected to be obtained by searching novel family members using this sequence. In fact, this approach has already identified the IL-11 receptor (Robb, L. et al., J. Biol. Chem., 1996, 271 (23) 13754-13761), leptin receptor (Gainsford T. et al., Proc. Natl. Acad. Sci. USA, 1996, 93 (25) p14564-8) and the IL-13 receptor (Hilton D.J. et al., Proc. Natl. Acad. Sci. USA, 1996, 93 (1) p497-501).

Paragraph beginning at page 3, line 11, has been amended as follows:

Until now, the inventors have been trying to search for a novel receptor using an oligonucleotide encoding the Trp-Ser-Xaa-Trp-Ser (SEQ ID NO:32) motif as a probe by plaque hybridization, RT-PCR method, and so on. However, because of reasons such as the oligonucleotide tggag (t/c) nnntggag (t/c) (SEQ ID NO:31) (where n is an arbitrary nucleotide) that encodes the motif being short having just 15 nucleotides, and the g/c being high, it was extremely difficult to strictly select only those in which the 15 nucleotides have completely hybridized under the usual hybridization conditions.

Paragraph beginning at page 3, line 25, has been amended as follows:

To solve these problems, and to estimate how many different hemopoietic receptor genes actually exist on the human genome, the inventors computer-searched sequences that completely

coincided with each probe using all capable oligonucleotide sequences encoding the above-mentioned Trp-Ser-Xaa-Trp-Ser (SEQ ID NO:32) motif as probes.

Paragraph beginning at page 30, line 1, has been amended as follows:

Figure 1 is a schematic diagram showing the results of BlastX search where the query was 180 nucleotides of 40861-41040 including 40952-40966, the only probe sequence within the AC002303. "#": For only NR8 the number was indicated by the nucleotide number. The underline of the NR8 sequence shows the portion corresponding to the exon. Other underlined sequences show identical amino acids (NR8 (SEQ ID NO:192), hTPOR (SEQ ID NO:193), hOBR (SEQ ID NO:194), hIL2Rb (SEQ ID NO:195), hIL7R (SEQ ID NO:196), hGM-CSFRb (SEQ ID NOs:197 and 198), mIL3Rb (SEQ ID NOs:199 and 200), hIL5Ra (SEQ ID NO:201), hIL9R (SEQ ID NO:202), hEPOR (SEQ ID NO:203), hIL2Rr (SEQ ID NO:204), hIL12R (SEQ ID NO:205), and hIL12Rb (SEQ ID NO:206).

Paragraph beginning at page 30, line 7, has been amended as follows:

Figure 2 is a schematic diagram showing the results of BlastX scanning of 180 nucleotides in both the 5' and 3' directions, where the search centered on the 180 nucleotides of 40861-41040 containing 40952-40966, the only probe sequence within the AC002303 (top: NR8 (SEQ ID NO:207), hIL6Ra (SEQ ID NO:208), hgp130 (SEQ ID NO:209), and rOBRb (SEQ ID NO:210); bottom: NR8 (SEQ ID NO:211), mIL9R (SEQ ID NO:212), and hIL9R (SEQ ID NO:213).

Paragraph beginning at page 30, line 17, has been amended as follows:

Figure 5 shows the nucleotide sequence and the amino acid sequence of NR8α cDNA (SEQ ID NOs:2 and 1, respectively). The arrows show the positions of primers used for RT-PCR. They are, SN1 (798-827), SN2 (894-923), AS2 (1055-1026), and AS1 (1127-1098) from the 5' side, in their order. For two bases at the 5' end of AS1, AC, which is derived from the genomic sequence, was used in place of CT.

Paragraph beginning at page 30, line 25, has been amended as follows:

Figure 7 shows the nucleotide sequence (SEQ ID NOs:4 and 6) and the amino acid sequence (SEQ ID NOs:3 and 5) of NR8β cDNA. Two possible open reading frames (ORF) are shown.

Paragraph beginning at page 30, line 29, has been amended as follows:

Figure 9 shows the nucleotide sequence and the amino acid sequence of NR8γ cDNA (SEQ ID NOs:8 and 7, respectively). The 177 amino acids inserted by selective splicing are underlined.

Paragraph beginning at page 31, line 10, has been amended as follows:

Figure 16 shows a comparison between amino acid sequences of human and mouse NR8β (SEQ ID NOs:3 and 19, respectively). The amino acid sequences where the two coincide are shadowed. Also, cysteine residues conserved in other hemopoietin receptors are displayed in boldface type within the sequence.

Paragraph beginning at page 31, line 14, has been amended as follows:

Figure 17 shows a comparison between amino acid sequences of human and mouse NR8γ (SEQ ID NOs:7 and 21, respectively). The amino acid sequences where the two coincide are shadowed. Also, cysteine residues conserved in other hemopoietin receptors and the WSXWS-Box are displayed in boldface type within the sequence.

Paragraph beginning at page 31, line 35, has been amended as follows:

Probe sequences (256 types) comprising the tggag(t/c)nnntggag(t/c) (SEQ ID NO:31) (where n is an arbitrary nucleotide) as the oligonucleotide encoding the Trp-Ser-Xaa-Trp-Ser (SEQ ID NO:32) motif were designed. These sequences enable the detection of almost all known hemopoietin receptors, except for the EPO receptor, TPO receptor, and the mouse IL6 receptor. Using each sequence as the query, the GenBank nr database was searched using the

BlastN (Advanced BlastN 2.0.4) program. Default values (Descriptions=100, Alignments=100) were used as parameters for the search, except for making the expectation value 100.

Paragraph beginning at page 32, line 23, has been amended as follows:

As a result of the secondary search by BlastX, 28 clones hit one or more known hemopoietin receptors (Table 1 to Table 8; top to bottom are SEQ ID NOs:33-187 – probe sequences are identical to the corresponding Hit site sequences).

Paragraph beginning at page 41, line 1, has been amended as follows:

Four clones out of these 28 clones (AC002303, AC003112, AL008637, and AC004004) hit several known hemopoietin receptors, however, AC004004 was excluded as it has a stop codon downstream three amino acids of the Trp-Ser-Xaa-Trp-Ser (SEQ ID NO:32) motif. Among the three remaining clones, AL008637 was thought to be a known receptor, GM-CSF receptor β. AC002303 is the BAC clone CIT987-SKA-670B5 derived from the 16p12 region of human chromosome no. 16 registered by TIGR group on June 19, 1997 and comprises the full-length of 131530 base pairs (Lamerdin, J.E., et al., GenBank Report on AC003112, 1997).

Paragraph beginning at page 41, line 10, has been amended as follows:

As shown in Fig. 1, a BlastX search (query: 180 nucleotides of 40861-41040 including tggagtgaatggagt (SEQ ID NO:107) (40952-40966), the only probe sequence within the AC002303) revealed that numerous hemopoietin receptors starting with the TPO receptor and leptin receptor show an evident homology, however, there were no known, database-registered hemopoietin receptors that completely matched the query sequence. Also, a BlastX scanning was done under the above conditions, by excising a sequential 180-residue nucleotide sequence in both the 5' and 3' directions, centering on the 180-residue nucleotide sequence mentioned above, and when this was used as a query, two sequences having a homology to known hemopoietin receptors were found in the regions 39181-39360 and 42301-42480, and were thought to be other exons of the same gene (Fig. 2).

Paragraph beginning at page 41, line 23, has been amended as follows:

A Pro-rich motif PAPPF (SEQ ID NO:188) was conserved in the 39181-39360 site, and a Box 1 motif in the 42301-42480 site. The 3' side exon adjacent to the exon containing the Trp-Ser-Xaa-Trp-Ser (SEQ ID NO:32) motif has a transmembrane domain, and this domain has a low homology with other hemopoietin receptors, and was not detected by the BlastX scan. These results suggested the possibility of a novel hemopoietin receptor gene existing in the above-described BAC clone CIT987-SKA-670B5.

Paragraph beginning at page 44, line 33, has been amended as follows:

As shown in Fig. 5 and Fig. 6, in the ORF of NR8α cDNA, the Met starting from nucleotide no. 441 is thought to be the start codon due to the presence of an inframe stop codon 39 bp upstream, and completes with two stop codons starting from nucleotide no. 1524. It has the features of, from the N terminus in order, a typical secretion signal sequence, a domain thought to be the ligand binding site containing a Cys residue conserved in other hemopoietic receptor members, a Pro-rich motif, Trp-Ser-Xaa-Trp-Ser (SEQ ID NO:32) motif, a transmembrane domain, a Box 1 motif thought to be involved in signal transduction, and such features of hemopoietin receptors. From the above results, the NR8 gene was thought to encode a novel hemopoietin receptor.

Table beginning at page 46, line 1, has been amended as follows:

Table 9

Exon	# in AC002303	# in NR8	Characteristics
1	<1	: 1-424	inframe stop codon
2	26334-26398	: 425-489	start codon, signal peptide
3	30625-30727	: 490-592	conserved Cys residue
4	33766-33965	: 593-792	conserved Cys residue, N-glycosylation site
5	39240-39394	: 793-947	Pro-rich motif (PAPPF; SEQ ID NO:188), N-glycosylation site
6	40820-40997	: 948-1125	gtWSEWSdp motif
7	41455-41554	: 1126-1225	transmembrane domain
8	42285-42366	: 1226-1307	Box1 (IWAVPSP; SEQ ID NO:189)
9a	44812-44909	: 1308-1405*	connects to exon 10, Box2-like sequence (PSTLEVYSCH; SEQ ID NO:190), nontypical exon/intron boundary
9b	44812-45922<	: 1308-2465**	double stop codons, Box2-like sequence (PSTLEVYSCH (SEQ ID NO:190), PAELVESDG (SEQ ID NO:191)), polyA
10	45441-45922<	: 1406-1934*	double stop codons, polyA

NR8 α*: exons 1+2+3+4+5+6+7+8+9a+10

NR8 β: exons 1+2+3+4+6+7+8+9a+10

(two alternative reading frames for soluble-type and transmembrane(-signal)-type)

NR8 γ**: exons 1+2+3+4+5+6+7+8+9b